

Figure 1: Illustrates the factors involved in maintaining the hemostatic balance. Any disturbance in this so-called hemostatic balance, or hemostatic potential, may result in bleeding or thrombosis. Too little hemostasis (decreased platelet function, hypo-coagulation, hyper-fibrinolysis) at the site of injury leads to persistent bleeding, while too much hemostasis (increased platelet function, hyper-coagulation, hypo-fibrinolysis) leads to the formation of an excessive thrombus with vascular obstruction and ischemia.

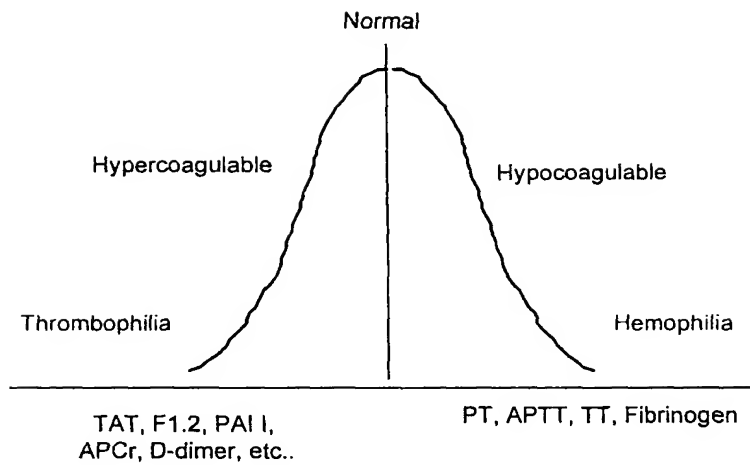


Figure 2 illustrates the conditions associated with being out of hemostasis and lists examples of assays used to assess the degree or presence of an imbalance.

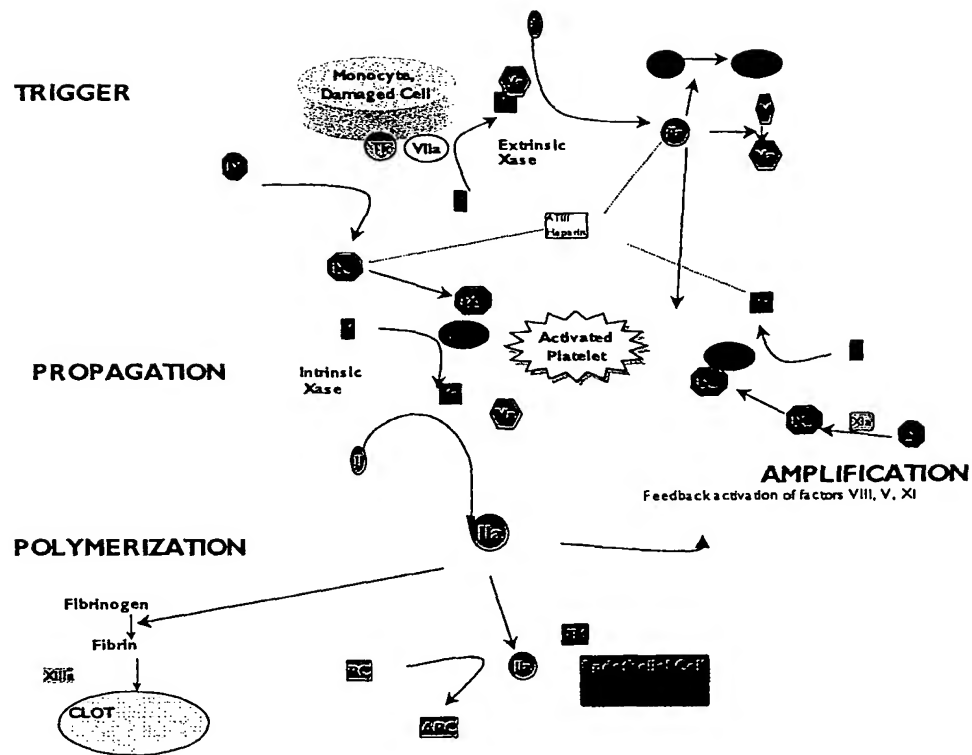


Figure 3: Coagulation Process

The process can be divided into four dependent phases, (1) the initiation phase, (2) the amplification phase, (3) the propagation phase and (4) the polymerization phase. All of the phases are effected by regulation and feedback processes referred to as anticoagulant pathways.

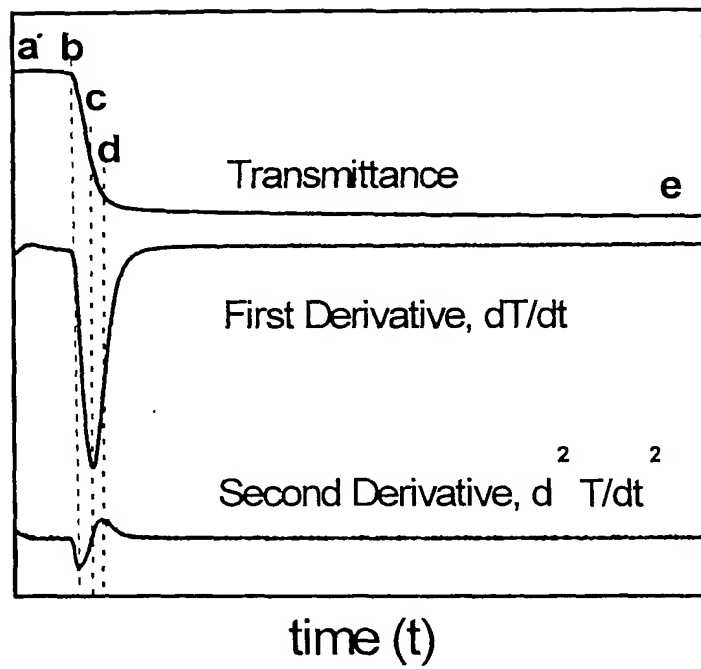


Figure 4 illustrates the optical data from a clotting assay and the first and second derivative calculated from that data.

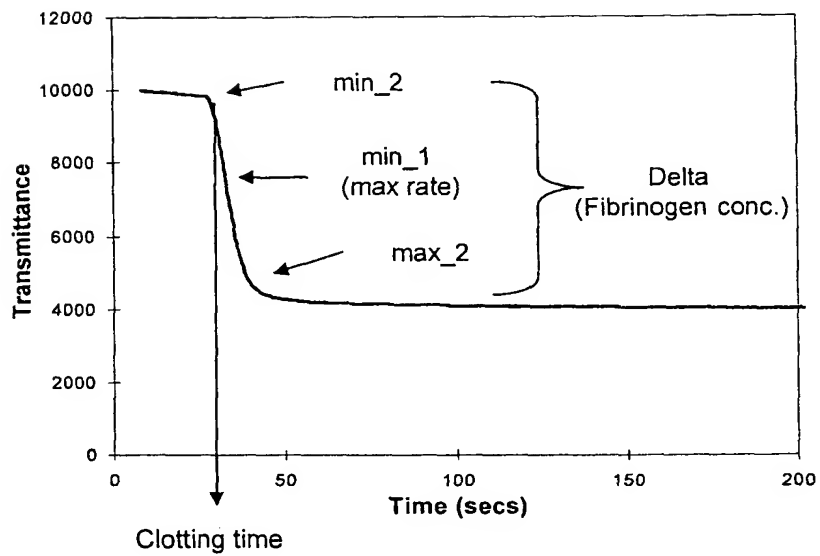


Figure 5 illustrates where min\_2, the time index of min\_2 (clotting time), min\_1, max\_2 and delta (related to fibrinogen concentration) are located in the optical data profile.

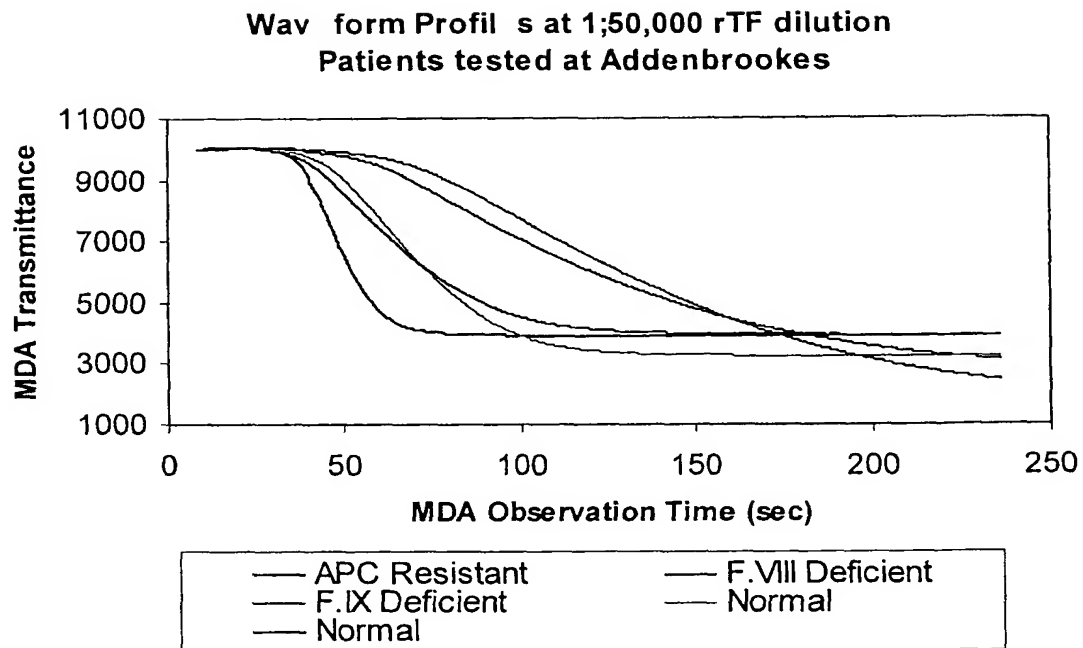


Figure 6: Examples of waveforms for the global screening assay at dilute tissue factor. The APC resistant , hypercoagulable specimen, generates a waveform that has essentially the same time of clot initiation compared to the normal. However, the rate of fibrin polymerization for the hypercoagulable specimen is significantly greater than that of the normal. The FVIII and FIX deficient hypocoagulable specimens, have only a slightly prolonged time of clot initiation whereas the rates of polymerization are significantly reduced when compared to normal or hypercoagulable specimens.

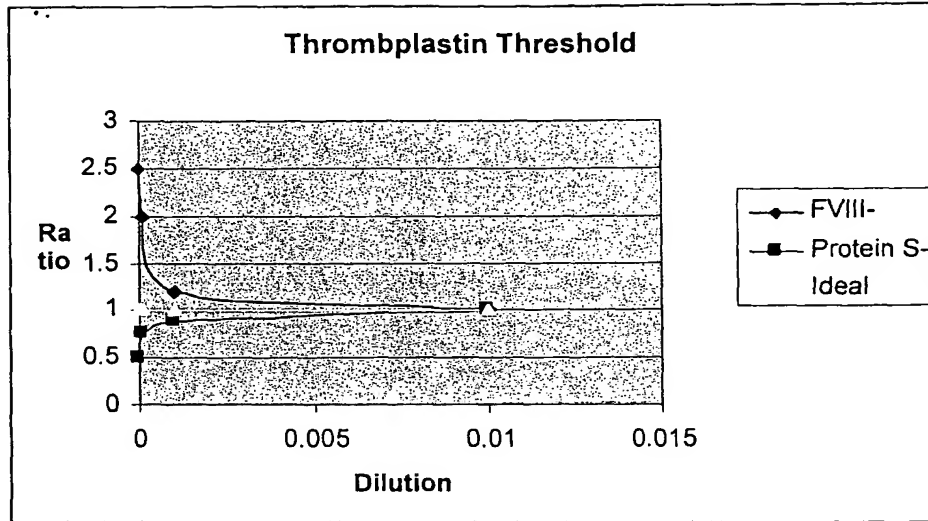


Figure 7 illustrates the change in ratio as a function of dilution for a FVIII deficient specimen and a Protein S deficient Specimen. The ratio values at 1:50,000 dilution of thromboplastin deviate from the response of the normal plasma. The hypocoagulable specimens is greater than 1 and the hypercoagulable specimen is less than 1 for this endpoint/ratio combination. Additionally, the abnormal specimens deviate from normal at different dilutions and in opposite directions.

**Influence of rTF Dilution on Min 1 Ratio  
Ratio Hypocoagulable to Normal Plasma, No TM**

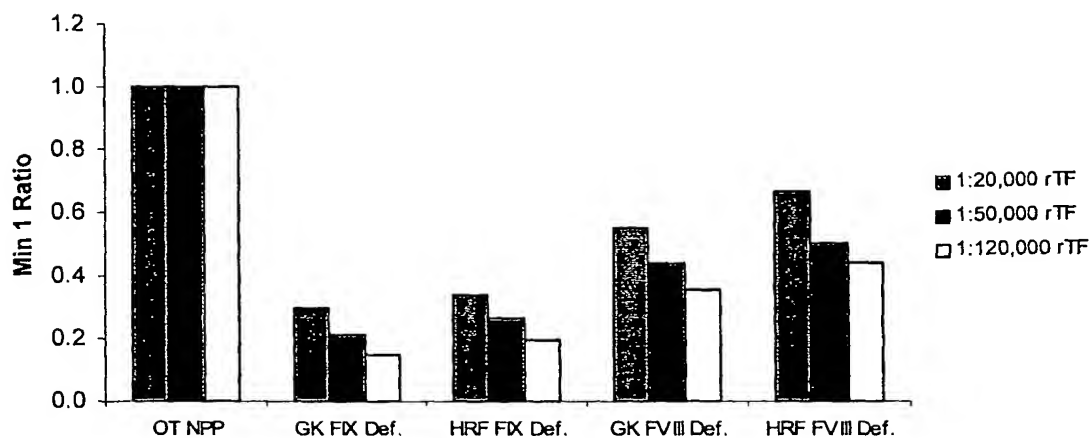


Figure 8 contains ratios of the min<sub>1</sub> values for hypocoagulable specimens at three dilutions of rTF compared to min<sub>1</sub> values of the same dilutions of normal plasma. All of the ratios of the hypocoagulable plasmas for all three dilutions are less than the normal response (values of <1). As the dilution increases, i.e. less tissue factor is provided, the difference in the ratios increases.



**Influence of rTF Dilution on Min 1 Ratio  
Ratio Hypercoagulable to Normal Plasma at 10nM TM**

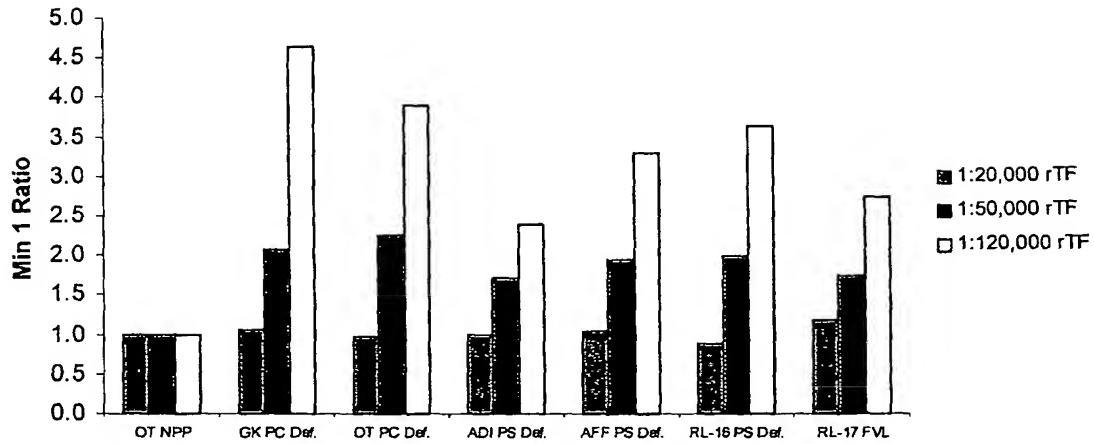


Figure 9 illustrates ratios of the min<sub>1</sub> values for hypercoagulable specimens at three dilutions of rTF in the presence of thrombomodulin compared to min<sub>1</sub> values for the same conditions for a normal plasma. All of the ratios of the hypercoagulable plasmas for all three dilutions are greater than the normal response (values of >1). As the dilution increases, i.e. less tissue factor is provided, the difference in the ratios increases.

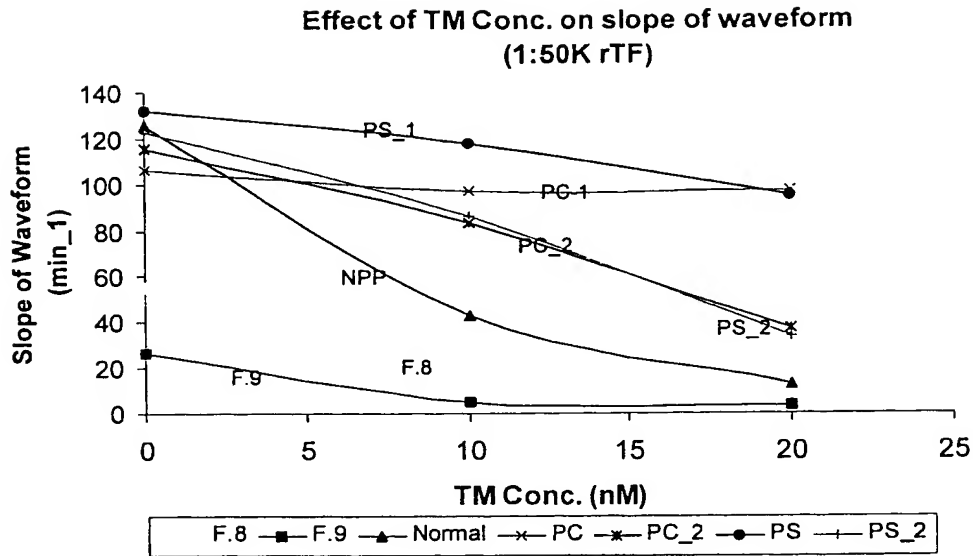


Figure 10 illustrates the effects on min\_1 values of varying tissue factor and thrombomodulin concentrations on results for hypercoagulable, hypocoagulable and normal plasmas. The data indicate that an optimal concentration can be defined to facilitate differentiation between normal, hypercoagulable and hypocoagulable plasmas. Additionally, other concentrations of tissue factor and thrombomodulin facilitate improvements in sensitivity and specificity for a particular condition at the expense of the sensitivity and specificity of another type of condition.